Time evolution of the Partridge-Barton Model

Roberto N. Onody*and Nazareno G. F. de Medeiros †

Departamento de Física e Informática

Instituto de Física de São Carlos

Universidade de São Paulo - Caixa Postal 369

13560-970 - São Carlos, São Paulo, Brasil.

Abstract

The time evolution of the Partridge-Barton model in the presence of the pleiotropic constraint and deleterious somatic mutations is exactly solved for arbitrary fecundity in the context of a matricial formalism. Analytical expressions for the time dependence of the mean survival probabilities are derived. Using the fact that the asymptotic behavior for large time t is controlled by the largest matrix eigenvalue, we obtain the steady state values for the mean survival probabilities and the Malthusian growth exponent. The mean age of the population exhibits a t^{-1} power law decayment. Some Monte Carlo simulations were also performed and they corroborated our theoretical results.

PACS numbers: 87.10.+e, 87.23.Kg, 87.23.Cc

*Eletronic address:onody@ifsc.sc.usp.br

†Eletronic address:ngfm@ifsc.sc.usp.br

1 Introduction

Early in life we perceive that everything around us, inanimate objects, animals and human beings undergo a variety of changes that accompany the passage of time. Everything suffers a progressive deterioration with time. This phenomenon is called ageing or senescence and it is characterized by a decline in the physical capabilities of the individuals. Several theories (see [1] and references therein) have been suggested to explain why there is senescence, when it occurs and what are the biological processes responsible for it. Usually, these theories are divided into three classes: biochemical, evolutionary and telomeric. The first invokes damages on DNA, cells, tissues and organs and connect senescence with imperfections of the biochemical processes. One kind of this biochemical imperfection is the presence of free radicals which can cause death of the cells or may even lead to cancer [2]. The evolutionary theory [3, 4], on the other hand, explains the senescence as a competitive result of the reproductive rate, mutation, heredity and natural selection. In the telomere hypothesis [5], senescence depends on the cumulative number of cell divisions. The replication of a normal cell is followed by a telomeric shortening. This acts as a counting mechanism which controls the number of divisions.

Evolutionary theories of ageing are hypothetico-deductive in character, not inductive. They do not contain any specific genetic parameter, but only physiological factors and constraints imposed by the environment. There are two kinds: the optimality theory and the mutational theory. In the optimality theory [6], senescence is a result of searching an optimal life history where survival late in life is sacrificed for the sake of early reproduction. For the mutational theory [4, 7], on the other hand, ageing is a process which comes from a balance between Darwinian selection and accumulation of mutations. The natural selection efficiency to remove harmful alleles in a population depends on when in the lifespan they come to express. Alleles responsible for lethal diseases that express late in life, escape from the natural selection and accumulate in the population, provoking senescence. Nevertheless, if the natural selection is too strong then deleterious mutations might not accumulate in the population and the eternal youth could be reached. An evolutionary model with such characteristics was

recently studied and solved by Onody and de Medeiros [8].

A simple evolutionary model of ageing is the Partridge-Barton model[9]. It was introduced to illustrate the optimality theories of ageing. Its principal feature is the inclusion of the antagonistic balance mechanism [10]. This mechanism arises out from processes which enhance the lifespan early in life, but have deleterious effects latter.

In this work, we find an exact solution for the whole dynamics of the Partridge-Barton model. When only deleterious somatic mutations and pleiotropy are present the time evolution of the model can be formulated in a matricial form. Explicit analytic expressions can be written for the mean survival probabilities and the growth rate. For large time t, the system behavior is dominated by the matrix largest eigenvalue. The existent integrals can be solved by the saddle point approximation, allowing us to determine precisely the steady state values of the survival probabilities. A time expansion for the population's mean age shows that it converges to a constant value according to a t^{-1} power law, a result which was first obtained by Ray [11]. All the results were confirmed by some Monte Carlo simulations that we performed.

2 The Partridge-Barton Model

In the Partridge-Barton model there are only three ages. The population consists of babies ($age = 0$), juveniles ($age = 1$) and adults ($age = 2$). The survival probabilities from infancy to juvenile is J_1 and from juvenile to adulthood is J_2. Reproduction is permitted only to juveniles and adults, with rates m_1 and m_2, respectively. Babies don't have offsprings and adults are eliminated from the population after reproduction.

The population grows at a steady rate r. The Malthusian growth exponent r is related to the other parameters of the model through a discrete version of the Euler-Lotka equation [12]

$$m_1 J_1 e^{-r} + m_2 J_1 J_2 e^{-2r} = 1. \tag{1}$$

The antagonistic pleiotropy [10] arises when the same gene is responsible for multiple effects. For example, genes enhancing early survival by promotion

of bone hardening might reduce later survival by promoting arterial hardening. Partridge and Barton implemented the basic ideas of the antagonistic pleiotropy by adopting the constraint, $J_1 + J_2^x = 1$, between the survival probabilities J_1 and J_2. The parameter x is a real positive number whose value depends on the kind of population we are dealing with. The pleiotropic condition states that it is impossible to sustain simultaneously both high juvenile and adult survivals. For the particular case in which $m_1 = m_2 = 1$ and $x = 4$, Partridge and Barton found $J_1 = 0.935$ and $J_2 = 0.505$ as the values which maximize the growth rate r.

Also the action of deleterious or helpful mutations can be added to the model. Using Monte Carlo simulations, Stauffer [13] studied the case in which the pleitropic constraint $J_1 + J_2^4 = 1$ is accompanied by random somatic mutations. His results clearly show that the survival probabilities J_1 and J_2 move rapidly to stationary values with $J_1 > J_2$. This fact means that the model exhibits senescence, in the sense that the adult survival is lower than the juvenile. In the absence of mutations, J_1 and J_2 tend towards 0.935 and 0.505 in accord with the Partridge-Barton conclusions. However, it is not clear how the system drives itself towards these optimal values.

3 Analytical Solution

In this section we obtain the exact time solution of the Partridge-Barton model in the presence of pleiotropy and somatic mutations.

Let $N_i(J_i, t)$ be the number of individuals at age i ($i = 0, 1, 2$) with survival probability between J_i and $J_i + dJ_i$ at time t. We choose, as initial condition, a population with the profile

$$N_i(J_i, 0) = N_0 \delta_{i,0}, \tag{2}$$

that is, in $t = 0$ there are only N_0 babies with the survival probabilities J_0 uniformly distributed in the interval $[0, 1]$.

At time t, all babies are equally submitted to somatic and deleterious mutations with strength α ($\alpha < 1$). Their survival probabilities J_0 are changed to $J_1 = \alpha J_0$. Subsequently, all these babies pass through natural selection in a

such way that, on average, the number of juveniles with survival probability J_1 at the instant $t+1$ is given by

$$N_1(J_1, t+1) = J_1 N_0(J_0, t). \tag{3}$$

Since the mutation is restricted to be *somatic*, each one of the $N_1(J_1, t+1)$ juveniles will give birth to exactly m_1 offspring with survival probability J_0.

Now, the probability with which a juvenile will reach adulthood must take into account the antagonistic pleiotropy and the somatic deleterious mutations. As pleiotropy is not affected by the somatic mutations, a juvenile with survival probability J_1 (formerly, a baby with survival probability J_0) will change its survival probability to $(1-J_0)^{1/x}$, where x is a real positive number and a measurement of the pleiotropic constraint. Under the action of a deleterious somatic mutation, described by a parameter β ($\beta < 1$, fixed), the new survival probability can be written as $J_2 = \beta(1-J_0)^{1/x}$. Submitting all juveniles to natural selection we get, on average, the number of adults with survival probability J_2 which is given by

$$N_2(J_2, t+1) = J_2 N_1(J_1, t). \tag{4}$$

Each one of these adults will generate m_2 descendants with survival probability J_0 since the mutations are *not inherited*.

In general, the number of babies with survival probability J_0 is given by

$$N_0(J_0, t) = m_1 N_1(J_1, t) + m_2 N_2(J_2, t), \quad for\ t \geq 1 \tag{5}$$

where $J_1 = \alpha J_0$ and $J_2 = \beta(1-J_0)^{1/x}$. If we substitute equation (5) into (3) we can write the following recursive matricial equation

$$\begin{pmatrix} N_1(J_1, t+1) \\ N_2(J_2, t+1) \end{pmatrix} = A \begin{pmatrix} N_1(J_1, t) \\ N_2(J_2, t) \end{pmatrix}, \tag{6}$$

where A is the matrix

$$A = \begin{pmatrix} m_1 J_1 & m_2 J_1 \\ J_2 & 0 \end{pmatrix}.$$

Iterating the equation above and using the initial condition, we get for $t \geq 2$

$$\begin{pmatrix} N_1(J_1, t) \\ N_2(J_2, t) \end{pmatrix} = J_1 N_0(J_0, 0) A^{t-2} \begin{pmatrix} m_1 J_1 \\ J_2 \end{pmatrix}, \tag{7}$$

with A^0 meaning the identity matrix.

The complete dynamics of the Partridge-Barton model can be obtained by diagonalizing the matrix A. We have, explicitly (for $t \geq 2$)

$$\begin{aligned} N_1(J_1,t) &= \frac{J_1 N_0(J_0,0)}{\sqrt{m_1^2 J_1^2 + 4 m_2 J_1 J_2}} \left[m_1 J_1 \left(\lambda_+^{t-1} - \lambda_-^{t-1} \right) \right. \\ &\left. + m_2 J_1 J_2 \left(\lambda_+^{t-2} - \lambda_-^{t-2} \right) \right], \end{aligned} \tag{8}$$

$$\begin{aligned} N_2(J_2,t) &= \frac{J_1 N_0(J_0,0)}{\sqrt{m_1^2 J_1^2 + 4 m_2 J_1 J_2}} \left[m_1 J_1 J_2 \left(\lambda_+^{t-2} - \lambda_-^{t-2} \right) \right. \\ &\left. + m_2 J_1 J_2^2 \left(\lambda_+^{t-3} - \lambda_-^{t-3} \right) \right], \end{aligned} \tag{9}$$

where

$$\lambda_\pm = \frac{m_1 J_1 \pm \sqrt{m_1^2 J_1^2 + 4 m_2 J_1 J_2}}{2} \tag{10}$$

are the eigenvalues of the matrix A, $J_1 = \alpha J_0$ and $J_2 = \beta(1 - J_0)^{1/x}$. Let us point out that the time evolution of the babies distribution $N_0(J_0, t)$, can be calculated using equations (5), (8) and (9). Having the expressions above, we can determine the evolution of many other quantities like the total number of inviduals at age i $N_i(t) = \int_0^1 N_i(J_i,t) dJ_i$ or their *mean survival probabilities* $\langle J_i \rangle(t) = \frac{\int_0^1 J_i N_i(J_i,t) dJ_i}{\int_0^1 N_i(J_i,t) dJ_i}$. The given *input parameters* are the initial population N_0, the birth rates (m_1 and m_2), the mutation strengths (α and β) and the pleiotropic constraint (x).

4 Asymptotic Limit

Before taking the asymptotic limit, we observe that λ_+ is the largest eigenvalue for *all* possible values of the input parameters. Once these parameters are fixed and $J_2 = \beta(1 - J_1/\alpha)^{1/x}$, λ_+ is in the last instance a function of J_1. From the equation (8) we have, asymptotically

$$N_1(J_1,t) \approx e^{t\ ln[\lambda_+(J_1)]}. \tag{11}$$

By integrating in J_1 the expression above, we can get the total number of juveniles $N_1(t)$. It is convenient to change the integration variable J_1 for a new variable y (a monotonically increasing function of J_1), $y = -cot(\pi J_1)$, such that

$$N_1(t) \approx \int_{-\infty}^{\infty} \frac{e^{t\ ln[\lambda_+(y)]}}{\pi(1+y^2)} dy. \tag{12}$$

For large time t, this integral can be evaluated by the saddle point approximation. We thus obtain

$$N_1(t) = A(\tilde{y}) \frac{e^{t\ ln[\lambda_+(y)]}}{\sqrt{t}}, \tag{13}$$

where $\tilde{y}$ is the value which maximize the eigenvalue λ_+ and $A(\tilde{y}) = \sqrt{\frac{\pi}{\frac{-1}{2\lambda_+}\frac{d^2\lambda_+}{dy^2}|_{y=\tilde{y}}}}$.

In the original paper of Partridge and Barton, the optimization process was achieved by a direct (and not well explained) maximization of the growth rate. Here, in our formalism, it is a simple and a natural consequence of taking the asymptotic time limit in the exact evolving equations. Further, the growth rate or the Malthusian exponent is simply given by $ln[\lambda_+(\tilde{y})]$.

To have deepest insight in the dynamics, let us determine the probability density $P_1(J_1, t)$ of finding a juvenile at time t with survival probability between J_1 and $J_1 + dJ_1$. It is given by

$$P_1(J_1, t) = \frac{N_1(J_1, t)}{\int_0^1 N_1(J_1, t) dJ_1} = \frac{N_1(J_1, t)}{N_1(t)} \approx \sqrt{t}\ e^{\ t\ ln[\frac{\lambda_+(J_1)}{\lambda_+(\tilde{J}_1)}]} \tag{14}$$

where we have used equations (11) and (13) and $\tilde{y} = -cot(\pi \tilde{J}_1)$. Clearly, at the asymptotic limit, the distribution probability $P_1(J_1, t \to \infty)$ approaches the Dirac delta function $\delta(J_1 - \tilde{J}_1)$ and the mean survival probability at age 1, is simply given by $\langle J_1 \rangle = \tilde{J}_1$. Similar results can be obtained for the ages 0 and 2. Another interesting quantity which can be calculated is the population mean age $\langle A \rangle(t)$ defined as $\langle A \rangle(t) = \frac{\sum_{i=0}^{2} i\ N_i(t)}{\sum_{i=0}^{2} N_i(t)}$. It is straightforward to show that

$$\langle A \rangle(t) = \frac{\gamma + 2}{\gamma(1+m_1) + (1+m_2)} + \left\{ \frac{2\gamma(1+m_1) + \gamma(1+m_2)}{2[\gamma(1+m_1) + (1+m_2)]^2} \right\} t^{-1} + O(t^{-2}) \tag{15}$$

where $\gamma = \frac{\lambda_+(\tilde{J}_1)}{\tilde{J}_2}$ with $\tilde{J}_2 = \beta(1 - \tilde{J}_1/\alpha)^{1/x}$. So we rederive, in a quite simple way, the power law decayment first found by Ray [11].

5 Discussion

We solved exactly in this paper the Partridge-Barton model under the action of arbitrary pleiotropic constraints and deleterious somatic mutations. Through a matricial formalism we were able to predict the complete time evolution of the population. We derived analytic expressions for the time dependence of the mean survival probabilities and the Malthusian exponent. Since for large time t the system behavior is controlled by the largest eigenvalue, it was possible to obtain the steady state values of the survival probabilities and to demonstrate, in a simple way, that the population mean age has a power law t^{-1} decayment to its final constant value.

For comparison with our analytical results, we also performed some Monte Carlo simulations. In these simulations, the natural selection is implemented by discarding any individual with survival probability smaller than a random number (generated from a uniform distribution). The deleterious somatic mutations and the antagonic pleiotropy can be easily incorporated into the computer program. More difficult is to avoid an explosion of the computer's memory due to the unlimited growth of the population. To take this problem into account, we resort to the Verhulst factor [12] which is commonly used in such circumstances.

In Figure 1 we put together the analytical solution and the Monte Carlo result. The exact solution was plotted by inserting equations (8, 9 and 10) into the expressions for the mean survival probabilities $\langle J_i \rangle(t)$ and by integrating them using the software Maple [14]. We conclude that the Monte Carlo simulations confirm very well the theoretical results.

Finally, let us to point out that, unfortunately, the technique developed here cannot be applied to the case in which mutations are hereditary. The main reason for this come from the fact that the equation (5) is no longer valid.

6 Acknowledgements

We acknowledge CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico) for the financial support.

References

[1] Bernardes A.T. in *Annual Reviews of Computational Physics IV*,pp 359-395, World Scientific Publishing Company, 1996.

[2] Kowald A. and Kirkwood T. B. L., J. Theor. Biol. **168**, 75 (1994).

[3] Rose M. R., *Evolutionary Theory of Aging*, Oxford University Press, Oxford, 1991.

[4] Charlesworth B., *Evolution in Age-Structured Populations*, Cambridge Univ. Press, 1994.

[5] Reddel R. R., BioEssays **20**, 977 (1998).

[6] Parker G. A. and Maynard Smith J., Nature **348**, 27 (1990).

[7] Medawar P. B., *An Unsolved Problem in Biology*, Lewis, London, (1952).

[8] Onody R. N. and de Medeiros N. G. F., Phys. Rev. E, **60**, 3234 (1999).

[9] Partridge L. and Barton N. H, Nature **362**, 305 (1993).

[10] Rose M. R., Heredity **48**, 63 (1982); Rose M. R., Theor. Pop. Biol. **28**, 342 (1985); Rose M. R., *Genetic Constraints on Adaptive Evolution* (ed. Loeschcke, V., Springer, Berlin), 91 (1987).

[11] Ray T. S., J. Stat. Phys. **74**, 929 (1994).

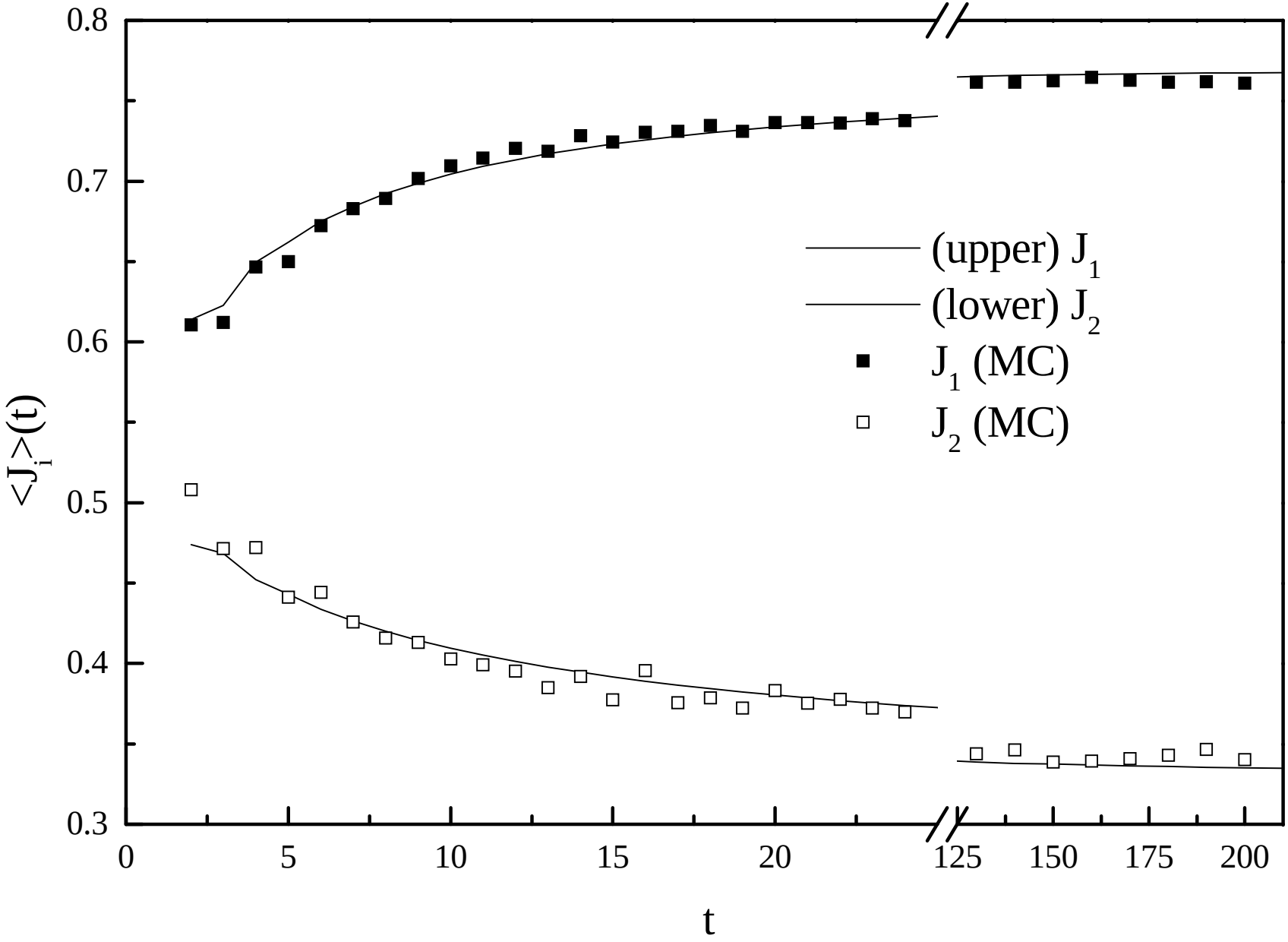
[12] Murray J.D.,*Mathematical Biology*, Springer-Verlag, Berlin, Heidelber, (1989).

[13] Stauffer D., Braz. J. Phys. **24**, 900 (1994).

[14] Maple is a registered trademark of Waterloo Maple Incorporation.

FIGURE CAPTION

Figure 1. The continuous lines correspond to the analytical solutions and the square symbols to the Monte Carlo simulations. We used $\alpha = 0.82$, $\beta = 0.67$, $x = 4$, $m_1 = m_2 = 1$ and $N_0 = 4000$. The steady state values are $\tilde{J}_1 = 0.77$ and $\tilde{J}_2 = 0.33$. There is senescence, i. e., $J_2 < J_1$.


0.8
0.7
0.6
0.5
0.4
0.3
<J_i>(t)
0
5
10
15
20
125
150
175
200
t
(upper) J_1
(lower) J_2
J_1 (MC)
J_2 (MC)